Gastric Cancer Risk in Patients With Premalignant Gastric Lesions: A Nationwide Cohort Study in the Netherlands

ANNEMARIE C. DE VRIES,* NICOLE C. T. VAN GRIEKEN,‡ CASPAR W. N. LOOMAN,§ MARIËL K. CASPARIE,* ESTHER DE VRIES,** GERRIT A. MEIJER,‡ and ERNST J. KUIPERS*¶

*Department of Gastroenterology and Hepatology, §Department of Public Health, ¶Department of Internal Medicine, Erasmus MC University Medical Center, Rotterdam; ‡Department of Pathology, VU University Medical Center, Amsterdam; and **Prismant, Utrecht, The Netherlands

See Watari J et al on page 409 in CGH.

Background & Aims: A cascade of precursor lesions (eg, atrophic gastritis, intestinal metaplasia, and dysplasia) precedes most gastric adenocarcinomas. Quantification of gastric cancer risk in patients with premalignant gastric lesions is unclear, however. Consequently, endoscopic surveillance is controversial, especially in Western populations. Methods: To analyze current surveillance practice and gastric cancer risk in patients with premalignant gastric lesions, all patients with a first diagnosis between 1991 and 2004 were identified in the Dutch nationwide histopathology registry (PALGA); follow-up data were evaluated until December 2005. Results: In total, 22,365 (24%) patients were diagnosed with atrophic gastritis, 61,707 (67%) with intestinal metaplasia, 7616 (8%) with mild-to-moderate dysplasia, and 562 (0.6%) with severe dysplasia. Patients with a diagnosis of atrophic gastritis, intestinal metaplasia, or mild-to-moderate dysplasia received re-evaluation in 26%, 28%, and 38% of cases, respectively, compared with 61% after a diagnosis of severe dysplasia (P < .001). The annual incidence of gastric cancer was 0.1% for patients with atrophic gastritis, 0.25% for intestinal metaplasia, 0.6% for mild-to-moderate dysplasia, and 6% for severe dysplasia within 5 years after diagnosis. Risk factors for gastric cancer development were increasing severity of premalignant gastric lesions at initial diagnosis (eg, severe dysplasia, hazard ratio 40.14, 95% confidence interval 32.2–50.1), increased age (eg, 75–84 years, hazard ratio 3.75, 95% confidence interval 2.8–5.1), and male gender (hazard ratio 1.50, 95% CI 1.3–1.7). Conclusions: Patients with premalignant gastric lesions are at considerable risk of gastric cancer. As current surveillance of these patients is inconsistent with their cancer risk, development of guidelines is indicated.

Gastric cancer represents the fourth most common cancer and second leading cause of cancer-related death worldwide. Although the incidence of gastric cancer has declined over the past decades, especially in Western countries, the mortality rate due to this disease remains high. As symptoms are frequently absent or only vague until the disease reaches an advanced stage, curative therapeutic options are usually limited at the time of diagnosis. Detection of gastric cancer at a curable stage substantially improves morbidity and survival. For instance, nationwide mass screening programs for gastric neoplasia in Japan have resulted in a higher detection rate of early gastric cancer. It has been suggested that cancer mortality has thereby been reduced. However, population screening is presumably less appropriate in regions with low incidences of gastric cancer, such as Western Europe and North America. Therefore, a more targeted approach seems necessary to reduce mortality in these regions. Identification and surveillance of individuals at high risk for gastric cancer may provide the basis for such a strategy.

An important risk factor for gastric cancer development is the presence of premalignant changes of the gastric mucosa. These lesions are involved in a widely accepted model leading to intestinal-type gastric carcinomas. In this multistep model of gastric carcinogenesis, *Helicobacter pylori* causes chronic inflammation of the gastric mucosa, which over years progresses through the premalignant stages of atrophic gastritis, intestinal metaplasia, and dysplasia to eventually gastric adenocarcinomas.

The detection and surveillance of patients with these premalignant lesions could potentially lead to early detection and treatment of advanced precursors and gastric carcinomas. Quantification of gastric cancer risk in patients with premalignant gastric lesions is

Abbreviations used in this paper: AG, atrophic gastritis; IM, intestinal metaplasia; Mild/Mod DYS, mild-to-moderate dysplasia; Severe DYS, severe dysplasia.
unclear, however, as studies evaluating the progression of premalignant lesions to gastric cancer have shown conflicting results. Reported progression rates to gastric cancer varied between 0% and 2% per year for atrophic gastritis. However, for intestinal metaplasia and dysplasia, progression rates to gastric cancer varied widely from 0% to 10% per year and from 0% to 73% per year, respectively. As a result, the efficacy of re-evaluation or surveillance of patients with premalignant gastric lesions remains highly controversial. In particular, in Western countries, only very limited recent data are available on this issue. Even for patients with gastric dysplasia, a condition carrying a presumed high cancer risk, clear guidelines on clinical management are lacking, and recommendations on timing and frequency of follow-up investigations vary widely. In this study, we therefore investigated the progression rates of premalignant gastric conditions to gastric cancer in a Western population, and in addition evaluated whether the surveillance practice of patients with these premalignant gastric lesions matches their cancer risk. The resulting data should provide a basis for decisions on gastric cancer surveillance practice in Western populations.

Materials and Methods

Histopathology Database

In the Netherlands, all histopathology and cytopathology reports are collected in a national archive (PALGA database), which has nationwide coverage since 1991. Each report can be tracked to an individual patient with a unique identifier, allowing follow-up on an individual basis regardless of whether treatment is received at the same or different institutes. Every record in the database contains a summary of the original pathology report and diagnostic codes similar to the Systemized Nomenclature of Medicine classification of the College of American Pathologists that are given by the pathologist who made the diagnosis. The diagnostic code contains a term indicating the anatomical location, type of sample, and a morphological term describing the finding (eg, "stomach*biopsy*intestinal metaplasia"). Details regarding the number and intragastric location of biopsies and presence of H pylori are not uniformly registered. The present study was based on data recorded in the PALGA database between 1991 and 2005.

Surveillance and Progression Analysis

Patients with histologically confirmed diagnoses of premalignant gastric lesions, (eg, atrophic gastritis, intestinal metaplasia, or dysplasia) were identified in the database (see Appendix). Only the most severe premalignant lesion at baseline (ie, the first observation of a premalignant lesion) was evaluated as the initial diagnosis.

Patients with either gastric or esophageal surgery or malignancy registered before or simultaneously with the first diagnosis of a premalignant gastric lesion were excluded from the cohort. In addition, a period of at least 1-year follow-up to receive a re-evaluation upper-gastrointestinal (GI) endoscopy was taken into consideration; consequently, patients with a first diagnosis in 2005 were excluded from analysis. For each patient, all summary texts and diagnostic codes concerning gastric biopsies from the first diagnosis of a premalignant gastric lesion to the end of the study period (December 2005) were retrieved.

In order to analyze surveillance, patients with a diagnosis of Barrett’s esophagus prior to or simultaneously with the diagnosis of a premalignant gastric lesion were excluded from analysis, as most of them participated in an endoscopic surveillance program for this indication. For diagnoses of esophageal and cardia adenocarcinomas, the pathology report of the surgical resection specimen was reviewed; only carcinomas of which the bulk was macroscopically located below the esophagogastric junction were evaluated as primary gastric cancer.

Statistical Analysis

As the PALGA registry does not contain the patients’ date of death, unless an autopsy had been performed, censoring because of death was imputed to evaluate the length of follow-up, using survival data from the general Dutch population (Dutch Cancer Registry personal communication, October 2007). Within each category of premalignant gastric lesions, intervals between initial and repeated upper GI endoscopies with biopsies and between initial premalignant and gastric cancer diagnosis were evaluated by Kaplan–Meier survival analysis;

Table 1. Baseline Characteristics of Our Study Population

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Atrophic gastritis</th>
<th>Intestinal metaplasia</th>
<th>Mild-to-moderate dysplasia</th>
<th>Severe dysplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>92,250</td>
<td>22,365 (24%)</td>
<td>61,707 (67%)</td>
<td>7,616 (8.3%)</td>
<td>562 (0.6%)</td>
</tr>
<tr>
<td>Age</td>
<td>Median: 65.7</td>
<td>60.7</td>
<td>66.5</td>
<td>68.7</td>
<td>75.3</td>
</tr>
<tr>
<td></td>
<td>25th–75th percentile: 53.1–75.5</td>
<td>46.4–73.3</td>
<td>54.9–75.8</td>
<td>56.8–77.2</td>
<td>64.9–81.4</td>
</tr>
<tr>
<td>Barrett’s esophagus (%)</td>
<td>1,934 (2.1%)</td>
<td>460 (2.1%)</td>
<td>1,219 (2.0%)</td>
<td>244 (3.2%)</td>
<td>11 (2.0%)</td>
</tr>
</tbody>
</table>
equality between the categories of premalignant gastric lesions was tested with the log-rank test. Univariate and multivariate Cox-regression analysis was performed to identify independent risk factors for progression of premalignant gastric lesions to more advanced gastric lesions in general or gastric cancer.

**Results**

A cohort of 92,250 patients with a first diagnosis of a premalignant gastric lesion was identified, with a 1:1 male-to-female ratio (Table 1). Median age at initial diagnosis was significantly higher with increasing severity of the categories of premalignant gastric lesions (P < .001) (Table 1). Women were significantly older than men at the initial diagnosis of atrophic gastritis (median age 63.2 years vs 57.8 years), intestinal metaplasia (68.7 vs 64.6), mild-to-moderate dysplasia (70.9 vs 66.9), and severe dysplasia (77.6 vs 72.1) (all P < .001). The mean age difference between men and women did not increase significantly with increasing severity of the categories of premalignant lesions (P = .35 univariate analysis of variance).

**Surveillance**

After excluding patients with Barrett’s esophagus, surveillance was evaluated in 90,316 patients using the unique identifier of each individual patient (Table 1). Patients with a diagnosis of gastric atrophy or intestinal metaplasia received at least 1 re-evaluation upper GI endoscopy with histological re-evaluation in 26% and 28% of cases, respectively, compared with 38% after a diagnosis of mild or moderate dysplasia and 61% of patients with severe dysplasia (P < .001) (Figure 1). In all categories of premalignant gastric lesions, patients who underwent subsequent histological re-evaluation were significantly younger than patients who did not (P < .001) (Figure 2). The mean interval between initial diagnosis and histological re-evaluation was 2.6 years (standard deviation [SD] 2.9) in patients with atrophic gastritis, 2.0 years (SD 2.6) for patients with intestinal metaplasia, 1.6 years (SD 2.4) in patients with mild-to-moderate dysplasia, and 0.4 years (SD 1.0) in patients with severe dysplasia (P < .001) (Figure 3). These findings show that the majority of patients with premalignant gastric lesions do not receive endoscopic follow-up, not even those with a diagnosis of dysplasia.

**Progression**

Histological follow-up data on the gastric mucosa were available on 26,538 patients (Figure 4). Progression to more advanced lesions overall, was significantly more common in patients with severe dysplasia as compared with patients with atrophic gastritis, intestinal metaplasia, and mild-to-moderate dysplasia (P < .001).

Progression to gastric cancer was evaluated for the whole cohort of 92,250 patients (Figure 5). During follow-up, 1470 patients developed gastric cancer at a median age of 73.5 years (SD 11.5) (61% men, 39% women). In total, 161 of these patients had at baseline been diagnosed with atrophic gastritis, 874 patients with intestinal metaplasia, 270 patients with mild-to-moderate dysplasia, and 165 patients with severe dysplasia. The age at diagnosis of gastric cancer was not significantly different.
between different diagnoses of premalignant gastric lesions at baseline ($P = .34$). Men were significantly younger at diagnosis of gastric cancer (median age, 72.3 years) as compared with women (75.5 years) ($P < .001$). The median interval between initial diagnosis and gastric cancer was 1.6 years (SD 3.2) in patients with atrophic gastritis, 0.90 years (SD 3.4) for patients with intestinal metaplasia, 0.45 years (SD 3.1) in patients with mild-to-moderate dysplasia, and 0.13 years (SD 2.7) in patients with severe dysplasia ($P < .001$). Within 1, 5, and 10 years of follow-up after initial diagnosis, gastric cancer was diagnosed in 0.3%, 0.6%, and 0.8% of patients with atrophic gastritis; 0.7%, 1.2%, and 1.8% of patients with intestinal metaplasia; 2.1%, 3.1%, and 3.9% of patients with mild-to-moderate dysplasia; and 24.9%, 29.5%, and 32.7% of patients with severe dysplasia ($P < .001$) (Figure 5). Men with intestinal metaplasia or mild-to-moderate dysplasia showed faster progression to gastric cancer as compared with women (both $P < .001$), whereas no significant difference was shown for men and women with atrophic gastritis or severe dysplasia ($P = .16$, respectively $P = .45$). The high number of gastric cancer diagnoses within 1 year of follow-up in patients with severe dysplasia suggests that these patients need to be re-examined shortly after diagnosis. Periodical surveillance seems indicated in all patients with gastric dysplasia; however, in patients with atrophic gastritis or intestinal metaplasia, risk of progression to gastric cancer is too low to recommend surveillance in all patients. Surveillance may be considered, however, at larger intervals in younger patients with
more severe or widespread atrophic gastritis and intestinal metaplasia.

**Risk Factors for Progression**

Within multivariate Cox-regression analysis, male gender was independently associated with an increased risk of progression to more advanced lesions overall (hazard ratio [HR] 1.55, 95% confidence interval [CI] 1.4–1.7) and with an increased risk of gastric cancer (HR 1.50, 95% CI 1.3–1.7), as compared with female gender (Table 2). In addition, increasing age at initial diagnosis was also independently associated with both progression to more advanced lesions and gastric cancer development. Moreover, gastric cancer risk increased significantly with the severity of premalignant gastric lesions at baseline and was clearly elevated in patients with intestinal metaplasia (HR 1.74, 95% CI 1.5–2.1), mild-to-moderate dysplasia (HR 3.93, 95% CI 3.2–4.8), and severe dysplasia (HR 40.14, 95% CI 32.2–50.1) as compared with patients with atrophic gastritis. Time period at initial diagnosis seemed an irrelevant risk factor for neoplastic progression, because a diagnosis in the period from 2001 to 2005 was associated with an increased risk of progression to more advanced lesions as compared with a diagnosis in the period from 1991 to 1995 (HR 1.83, 95% CI 1.6–2.1); however, gastric cancer risk was lower (HR 0.82, 95% CI 0.7–1.0). These findings show that male patients with premalignant gastric lesions carry a higher risk of gastric cancer development than female patients. Gastric cancer risk is especially elevated at an older age and after a diagnosis of more severe lesions at baseline.

**Discussion**

This large, nationwide study shows that patients with premalignant gastric lesions carry a significant risk of gastric cancer within 10 years of follow-up (Figure 6). However, in Dutch clinical practice, which is likely to be representative for many Western countries, surveillance of these patients is regularly omitted, even in patients with overt dysplasia.

Within 5 years of follow-up, the annual incidence of gastric cancer in our Western population was 0.1% for patients with atrophic gastritis, 0.25% for intestinal metaplasia, 0.6% for mild-to-moderate dysplasia, and 6% for severe dysplasia. These observations are in line with the multistep cascade described by Correa.\(^4,13,14\) Although this multistep cascade has been accepted for many years, quantification of gastric cancer risk in men and women with different premalignant gastric lesions has remained unclear, in particular in Western populations. Previous cohort studies had limited sample sizes, used older histological classifications, in part specifically focused on patients with pernicious anemia, and the first studies used blindly obtained instead of endoscopic gastric biopsy samples. For these reasons, those data are of limited use for current daily practice. As a result, endoscopic surveillance of premalignant gastric lesions is highly controversial. The present data provide important insights in cancer risk and current management of patients with premalignant gastric lesions. They show that surveillance with endoscopy and biopsy sampling is relevant in patients with more advanced premalignant lesions and may lead to early detection of cancer. The improved prognosis

---

**Table 2. Risk Factors for Progression to Advanced Precursor Lesions and Gastric Cancer in Univariate and Multivariate Cox-Regression Analysis**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Overall progression</th>
<th>Gastric cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR univariate</td>
<td>95% CI</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.29 (1.2–1.4)</td>
<td>1.55 (1.4–1.7)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–44 years</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>45–54 years</td>
<td>0.97 (0.8–1.2)</td>
<td>1.06 (0.9–1.3)</td>
</tr>
<tr>
<td>55–64 years</td>
<td>1.43 (1.2–1.7)</td>
<td>1.62 (1.4–1.9)</td>
</tr>
<tr>
<td>65–74 years</td>
<td>2.04 (1.8–2.4)</td>
<td>2.33 (2.0–2.7)</td>
</tr>
<tr>
<td>75–84 years</td>
<td>3.46 (3.0–4.1)</td>
<td>3.94 (3.4–4.6)</td>
</tr>
<tr>
<td>&gt;85 years</td>
<td>5.34 (4.3–6.7)</td>
<td>6.45 (5.1–8.1)</td>
</tr>
<tr>
<td>Histopathology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrophic gastritis</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Intestinal metaplasia</td>
<td>0.52 (0.5–0.6)</td>
<td>0.43 (0.4–0.5)</td>
</tr>
<tr>
<td>Mild-to-moderate dysplasia</td>
<td>0.68 (0.6–0.8)</td>
<td>0.53 (0.5–0.6)</td>
</tr>
<tr>
<td>Severe dysplasia</td>
<td>6.11 (5.2–7.2)</td>
<td>3.57 (3.0–4.2)</td>
</tr>
<tr>
<td>Period of initial diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1991–1995</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>1996–2000</td>
<td>1.32 (1.2–1.4)</td>
<td>1.26 (1.2–1.4)</td>
</tr>
<tr>
<td>2001–2004</td>
<td>2.02 (1.8–2.3)</td>
<td>1.83 (1.6–2.1)</td>
</tr>
</tbody>
</table>
after such early detection underlines the importance of development of surveillance guidelines.

As only a small proportion of patients with atrophic gastritis or intestinal metaplasia eventually develops gastric cancer, endoscopic follow-up of all patients with these lesions is not indicated but should be limited to patients at high risk. Previous studies have identified the intragastric location, severity, and distribution of atrophy and intestinal metaplasia, as well as the concomitant presence of associated lesions, especially, mucosa-associated lymphoid tissue (MALT) lymphoma or gastric ulcer, as markers of increased risk.\(^9,15,16\) Furthermore, the risk is influenced by \(H\) pylori virulence factors, a family history of gastric cancer, host genetics, and environmental factors (cigarette smoking, in particular).\(^17–21\)

From our data, we can conclude that the cancer risk in patients with mild-to-moderate gastric dysplasia is similar to or even considerably higher than the risk of cancer after removal of colonic adenomas, as well as in patients with Barrett's esophagus or long-standing inflammatory bowel disease.\(^22–24\) It is remarkable that surveillance guidelines have been widely accepted for these conditions, whereas similar guidelines for follow-up of patients with dysplastic gastric lesions are lacking. Such a guideline should include the need for follow-up biopsy, confirming the presence of dysplasia, as well as recommendations on \(H\) pylori eradication.

Patients with severe dysplasia, currently classified as noninvasive high-grade neoplasia according to the revised Vienna classification, are at high risk to develop gastric cancer within 2 years of follow-up.\(^25,26\) This finding is in line with the results of previous studies.\(^27–29\) Given this high cancer risk, thorough endoscopic and histological re-evaluation shortly after initial diagnosis is strongly indicated.\(^30\) New endoscopic techniques, such as magnification endoscopy and narrow band imaging may help the identification of neoplastic lesions, enable targeted biopsies, and assist endoscopic resection.\(^30–32\) All patients with identified dysplasia should be kept under strict surveillance with repeated multiple biopsy sampling. Preliminary data show that endoscopic resection of early neoplastic lesions needs to be considered.\(^33\)

This study identifies male gender as an important independent risk factor for progression to more advanced lesions and gastric cancer. Moreover, men showed a significantly faster progression of premalignant lesions to gastric cancer as compared with women (\(P < .001\)). This observation remained unchanged after stratifying patients by age. In addition, premalignant gastric lesions were diagnosed at a significantly higher age in women. These findings are in accordance with the male predominance in gastric cancer incidence and imply that women not only enter the carcinogenic cascade at an older age but also progress slower through subsequent stages. The explanations for these differences are unknown; however, plausible explanations are an increased use of non-steroidal anti-inflammatory drugs, less smoking, a lower prevalence of virulent \(H\) pylori strains, and a preventive effect of female hormones.\(^34–36\) However, the influence of sex hormones is contradicted by the fact that differences in progression rate to gastric cancer between genders persisted after menopause.

Although this study describes a large nationwide cohort, potential weaknesses warrant consideration. First, it was impossible to evaluate clinicians' motivation to choose for or against surveillance. The majority of subjects never received endoscopic follow-up, not even those with advanced lesions at a young age. This supports the hypothesis that clinicians are insufficiently aware of the cancer risk of these patients and remain uncertain about the clinical management in the absence of guidelines. Second, as patients were treated in all hospitals throughout the country, differences in biopsy sampling protocol and histological assessment cannot be excluded.\(^37\) Nevertheless, for grading of gastritis, it has long been routine to obtain antrum biopsies. It is at this same location that premalignant lesions predominate, with spread along the lesser curvature.\(^38\) As we have categorized patients according to the most severe lesion, this is likely to reflect the true status of their gastric mucosa. The finding that this categorization correlates strongly with gastric cancer risk supports this assumption. In addition, the large number of patients in this study generously compensates for biopsy sampling and observer variation. Third, to evaluate progression rates to gastric cancer, a virtual life expectancy was calculated for all patients without follow-up until December 2005 based on the life expectancy of the general population. This assumption may have led to a slight underestimation of gastric cancer risk, however, as a population undergoing endoscopy tends to have increased comorbidity and mortality rates. In particular, risk factors for the development of premalignant gastric lesions may have caused a higher overall mortality rate.\(^15,21,39\) Fourth, it was impossible to evaluate the influence of \(H\) pylori eradication on the reported progression rates of premalignant gastric lesions in our study population. During most of our study period, however, the presence of premalignant gastric lesions was not an indication for \(H\) pylori eradication. Also, previous studies have suggested that \(H\) pylori eradication may only have a very limited effect on subsequent gastric cancer incidence in patients with pre-existent premalignant gastric lesions, such as our population.\(^40–43\) For these reasons, it is unlikely that the observed annual cancer incidences were strongly influenced by \(H\) pylori eradication treatments in our population. Finally, an important problem in studies evaluating progression of premalignant lesions is the occurrence of sampling errors (ie, the inability to biopsy the exact same intragastric location twice), which is even more relevant when the preneoplastic lesion has a patchy distribution.\(^44\) In patients with dysplasia, lesions are
more likely to be visible endoscopically, thus allowing for targeted biopsy sampling. In contrast, atrophic gastritis and intestinal metaplasia are mostly diagnosed in random biopsies, reflecting the background status of the gastric mucosa in these patients. Our results show that this background status allows differentiation into risk categories for gastric cancer.

Judgment on the efficacy of surveillance of patients with premalignant gastric lesions requires consideration of burden for patients, costs, and capacity of hospital care. Detailed research into these aspects is required to identify individuals who should be offered surveillance. In case surveillance is performed, more research is needed on the exact design of strategies, including the most optimal endoscopic surveillance frequency, techniques, and biopsy sampling protocols.

In conclusion, gastric cancer risk in patients with atrophic gastritis, intestinal metaplasia, and dysplasia of the stomach increases significantly with progressive severity of the lesions. The occurrence and progression of these lesions are more pronounced in men than in women. Most importantly, the risk of cancer is comparable or even higher in patients with premalignant gastric lesions than in patients with other premalignant gastrointestinal conditions, which are routinely monitored. Therefore, follow-up should also be seriously considered in patients with premalignant gastric lesions. As current surveillance of premalignant gastric lesions is discrepant with the substantial gastric cancer risk of these lesions, development of clinical guidelines on endoscopic surveillance or treatment of premalignant gastric lesions is strongly indicated. Our data show that routine endoscopic surveillance at short intervals is warranted in patients with gastric dysplasia, whereas surveillance at longer intervals should be considered for patients with atrophic gastritis and intestinal metaplasia. Knowledge of detailed individual risk of progression to gastric cancer is important and requires further investigation.

Appendix

PALGA diagnosis codes used in the analysis:
Atrophic gastritis: M58000, M58001, M58010
Intestinal metaplasia: M73000, M73200, M73320, M73321, M73300
Dysplasia: M74000, M74006, M74007, M74008, M74009
Gastric adenocarcinomas: M80011, M80101, M80102, M81403, M80103, M84803, M81443, M81453, M84903, M82113, M80503, M82603, M69360, M80104, M80105, M80123, M80193, M80203, M81404, M80213

References

Received September 12, 2007. Accepted January 10, 2008.

Address requests for reprints to Annemarie C. de Vries, MD, Department of Gastroenterology and Hepatology, Erasmus MC, Room L-462, P.O. Box 2040, 3000 CA Rotterdam, the Netherlands. e-mail: A.C.deVries@erasmusmc.nl; fax: (31) 0104632793.

All authors have contributed to the conception and design and interpretation of the data, and the drafting of the article or critical revision. A.C. de Vries and C.W.N. Looijen analyzed the data. The authors have no conflict of interest to disclose.

The authors wish to thank H. van Dekken, pathologist, for the photographic illustrations.